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ORIGINAL PAPER

Quality of life in children with undiagnosed and diagnosed asthma

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Abstract This study describes the impact of undiagnosed and diagnosed asthma on quality of life in schoolchildren aged 7–10 years and their caregivers in a cross-sectional community-based study. Diagnosed asthma was defined as the parents' confirmation of a physician's diagnosis of asthma. Undiagnosed asthma was defined by asthma symptoms combined with airway reversibility or bronchial hyperresponsiveness. Quality of life was evaluated in all children with asthma and a sample of healthy controls by the Pediatric Asthma Quality of Life Questionnaire, and by the Paediatric Asthma Caregiver's Quality of Life Questionnaire. We studied the impact of breathing problems on school absence. Compared with healthy controls, quality of life scores among children and their caregivers were lower if the child had asthma ($P<0.05$), with lowest scores in diagnosed asthma ($P<0.05$ compared with undiagnosed asthma). Children with asthma reported more school absence ($P<0.05$), with highest absence rate in those with diagnosed asthma. In conclusion, both undiagnosed and diagnosed asthma have a significant impact on the quality of life of both children and their caregivers.

Keywords Asthma · Children · Quality of life

Abbreviations

UDA	undiagnosed asthma
DA	diagnosed asthma
HC	healthy controls
BHR	bronchial hyperresponsiveness
BD	bronchodilator
PAQLQ	Pediatric Asthma Quality of Life Questionnaire
PACQLQ	Paediatric Asthma Caregiver's Quality of Life Questionnaire
FEV_1	forced expiratory volume in 1 s

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Introduction

In Western European and affluent countries, asthma is the most common chronic disease, with prevalence rates of up to 32% [1]. Since 1980 numerous studies have shown that asthma in children is underdiagnosed and subsequently

undertreated [3, 6, 9, 17, 21, 23]. Recent data show that underdiagnosis is still a problem [8]. Chew et al. [5] reported that 49% of all children with asthma-like symptoms had not been diagnosed with asthma and Joseph et al. [10] reported a prevalence of undiagnosed asthma of 11.7%.

Information about the quality of life in children with mild to moderate asthma is scarce. The AIRE (Asthma Insight and Reality) study showed only partial effectiveness of asthma care in daily life [20]. Only 5.8 % of children met all criteria for asthma control and over one third of children had daytime symptoms at least once a week despite adequate treatment. For undiagnosed asthma, Yeatts et al. [24] concluded that undiagnosed frequent wheezers report more sleep disturbances, school absence and activity limitations than diagnosed asthmatics; however, their study lacked objective measures to diagnose asthma.

The present study describes the impact of having asthma on daily life in a community-based population of school-children with or without a physician's diagnosis of asthma. For this we evaluated the quality of life both in children and their caregivers, as well as the occurrence of asthma symptoms and their effect on school absence.

Materials and methods

Population and study protocol

The study was conducted in 41 out of 44 primary schools in four cities in the south of the Netherlands. We asked all children aged 7–10 years and their parents to participate in our study. All participating parents completed a questionnaire on respiratory symptoms, demographic and household characteristics. All participating children were invited for lung function testing with assessment of reversibility to salbutamol. Children with asthma symptoms in the past 12 months or reversible airway obstruction were invited for bronchial challenge with hypertonic saline. Based upon results from questionnaires, airway reversibility and bronchial hyperresponsiveness (BHR) children were identified as 'diagnosed asthma' (DA), 'undiagnosed asthma' (UDA), 'healthy controls' (HC), 'asymptomatic airway reversibility', or 'asthma symptoms only. Quality of life was assessed in all children with asthma (diagnosed and undiagnosed) and a sample of healthy controls that were randomly selected from the same class as children with asthma. Parents received a letter with the results of the symptom questionnaire and lung function 2 weeks after finishing the study protocol.

Approval for the study was obtained from the central Committee on Research involving Human Subjects (CCMO) in the Hague, the Netherlands. Informed written consent was obtained from the parents of all children.

Questionnaire

Parents completed a questionnaire that included the ISAAC core questions on symptoms of asthma, rhinitis and eczema [2]. Additional data were collected on household characteristics. Asthma symptoms were defined as wheeze or a dry cough at night in the past 12 months.

Spirometry and reversibility

Maximal flow-volume curves were measured using a hand-held spirometer (Vitalograph, Buckingham, UK) according to the ERS guidelines [18]. A minimum of two technically acceptable baseline flow-volume curves were performed and the highest of two reproducible (within 5%) measurements of forced expiratory volume in 1 s (FEV_1) was recorded as baseline FEV_1. Subsequently, 800 μg of salbutamol was administered via a metered dose inhaler using a volumatic spacer (GSK, Uxbridge, UK). Airway reversibility was defined as an increase of FEV_1 of ≥10% of the predicted value 10 min after administration of salbutamol.

Hypertonic saline testing

Bronchial hyperresponsiveness was assessed by inhalation challenge with nebulized hypertonic (4.5%) saline using an ultrasound nebulizer (Klava 2000/4000, Klava Eltromed, Bielefeld, Germany) according to the ISAAC protocol. BHR was assessed on a different day than the spirometry [22]. All children were asked to withhold all asthma medications for at least 12 h beforehand. Children with a baseline FEV_1 ≤75% were excluded. The children inhaled the saline for periods of increasing duration: 0.5, 1, 2, 4, and 8 min. FEV_1 was measured 1 min after each inhalation period and the next inhalation period started after 3 min. Bronchial challenge was stopped if FEV_1 had fallen at least 15% from baseline or if the total inhalation period of 15.5 min had been completed. A child was defined as having BHR if FEV_1 had dropped by ≥15% from baseline during the inhalation challenge.

Daily impact of asthma

Quality of life was measured with the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) for children, and with the Pediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) for their caregivers [11, 12]. For both questionnaires scores range from 1 to 7, with 7 indicative of maximal quality of life. The PAQLQ consists of three domains, i.e. emotions, activity and symptoms. The PACQLQ consists of two domains, i.e. the emotions domain and activity domain.

School absence because of respiratory disease was evaluated by the question: "How often was your child absent from school due to breathing problems in the last 12 months?" Additionally, children completed a 5-day diary addressing the following question: "Did you feel different or left out today because of shortness of breath, coughing or wheezing?"

Definitions

A child was considered having diagnosed asthma if the parents confirmed that their child had physician-diagnosed asthma in the last 12 months. A child was considered having undiagnosed asthma if the child had (1) no physician-diagnosed asthma in the last 12 months, (2) asthma symptoms (wheeze or dry cough) in the last 12 months, and (3) either had reversible airway obstruction or BHR. Healthy controls (HC) had no asthma diagnosis or symptoms in the last 12 months, and no reversible airway obstruction. The remainder children comprised those with asymptomatic airway reversibility (airway reversibility without asthma diagnosis or symptoms), and children with asthma symptoms only.

Data analysis

All data of the questionnaires were double-entered into the database using Microsoft Access software. Chi-square tests and ANOVA with a Bonferroni post-hoc test were used to analyse differences between the groups. Data were analysed using the statistical package SPSS version 11.0.

Results

Participants

Of 44 eligible schools, 41 participated in the study. Reasons for non-participation were recent involvement in another study (n=2) and school policy never to participate in medical studies (n=1). We invited 2,745 children and their parents to participate in the study in the period September 2002 to April 2005, of which 1758 (64%) gave informed consent to participate. We excluded 144 children from further analysis; reasons for excluding were missing questionnaire data (n=60), refusal to participate in bronchial challenge testing (n=31), not completing the bronchial challenge test due to nausea or coughing (n=3) or inability to meet technical conditions (n=50).

Diagnosis and demographics

The final study population comprised 1,614 children, of whom 81 (5.0%) had diagnosed asthma and 130 (8%) undiagnosed asthma according to our criteria. Asymptomatic airway reversibility occurred in 14% and 19% had asthma symptoms only. Of the remaining healthy controls, we randomly selected 202 children for assessment of quality of life. Table 1 presents the characteristics of the study population. Children with diagnosed asthma more frequently had a father with asthma compared with the children with undiagnosed asthma (P<0.05) and healthy controls, whereas having a mother with asthma occurred more frequently in children with both diagnosed and undiagnosed asthma (P<0.001).

Table 2 presents clinical characteristics of the patient groups. Wheeze in the last 12 months occurred most frequently in diagnosed asthma (86%) compared with undiagnosed asthma (56%) and healthy controls (0%) (P<0.001 for all comparisons). In contrast, children with undiagnosed asthma had the lowest baseline FEV_1, which showed the greatest increase after inhalation of salbutamol (9%, 5%, 2%, respectively; UDA vs HC; P<0.001, UDA vs DA; P=0.07). Furthermore airway reversibility and BHR occurred more frequently in children with undiagnosed asthma than in children with diagnosed asthma and healthy controls (reversibility 52%, 24% and 0% for, respectively, UDA, DA and HC, P<0.001; respectively, 73%, 47%, and 11% for BHR, P<0.001).

Table 1 Characteristics of the patient groups

	Undiagnosed asthma (n=130)	Diagnosed asthma (n=81)	Healthy controls (n=202)
Gender, n (%)			
Male	73 (56)	47 (58)	100 (50)
Female	57 (44)	34 (42)	102 (50)
Mean age±SD (years)	9.4±0.7	9.4±0,8	9.4±0.7
Mother asthma ever, n (%)	19 (17)	16 (23)	4 (2)
Father asthma ever, n (%)	7 (5)	11 (16)	12 (7)
Mother current smoker, n (%)	26 (20)	10 (14)	41 (22)
Father current smoker, n (%)	30 (26)	17 (24)	42 (22)
Mother's education			
Low, n (%)	17 (15)	14 (20)	33 (17)
Moderate, n (%)	56 (49)	34 (48)	95 (50)
High, n (%)	41 (36)	23 (32)	62 (33)
Father's education			
Low, n (%)	20 (20)	16 (24)	37 (20)
Moderate, n (%)	41 (40)	22 (32)	65 (35)
High, n (%)	40 (40)	30 (44)	82 (45)
Pet ownership			
Currently, n (%)	78 (70)	39 (54)	117 (61)
Ever, n (%)	89 (80)	55 (76)	142 (74)

Table 2 Clinical characteristics of the patient groups

	Undiagnosed asthma	Diagnosed asthma	Healthy controls	*P* value
Symptoms in last 12 months				
Wheeze, *n* (%)	72 (56)	70 (86)	0 (0)	<0.001[a, b, c]
Dry cough at night, *n* (%)	90 (71)	54 (70)	0 (0)	<0.001[b, c]
Lung function parameters				
Mean baseline FEV_1 % predicted	94	98	100	<0.001[b]
Mean baseline FVC % predicted	89	95	95	<0.05[a, b]
Change in FEV_1 after BD (%)	+9	+5	+2	<0.001[b]
Reversibility ≥10%, *n* (%)	67 (52)	19 (24)	0 (0)	<0.001[a, b, c]
BHR, *n* (%)	93 (73)	38 (47)	21 (11)	<0.001[a, b, c]
Inhaled corticosteroids	12 (9%)	60 (74%)	0 (0)	

[a] Significant difference between undiagnosed asthma and diagnosed asthma
[b] Significant difference between undiagnosed asthma and healthy controls
[c] Significant difference between diagnosed asthma and healthy controls

Impact on daily life

Table 3 presents data on the quality of life of children and their caregivers. For all domains, children with diagnosed or undiagnosed asthma had lower quality of life scores than healthy controls ($P<0.05$). Quality of life in children with diagnosed asthma was lower than in children with undiagnosed asthma for all domains ($P<0.05$). Quality of life scores in caregivers showed a similar pattern. Irrespective whether diagnosed or not, asthmatic children showed a lower score on the activity domain than their caregivers did ($P<0.05$).

We estimated the effect on daily function by a 5-days' symptom diary and evaluation of school absence in the last 12 months. Children with diagnosed asthma reported twice as many symptoms in the diary than children with undiagnosed asthma (11% and 5%, respectively, $P<0.05$). Children with diagnosed and undiagnosed asthma were more than 1 week absent from school in the last 12 months due to respiratory symptoms than healthy controls, i.e. 31%, 17%, and 0%, respectively ($P<0.001$) (Table 4). Because corticosteroid treatment may affect lung function and quality of life score, we repeated the analysis after excluding children with undiagnosed asthma that used inhaled corticosteroids. Results remained essentially the same.

Discussion

In the present study, we found a lower quality of life on all domains in children with diagnosed and undiagnosed asthma compared with healthy children. We found the same results for their caregivers. Lowest scores were observed in children with diagnosed asthma. Similarly, symptoms during five consecutive days and school absence in the last 12 months occurred more frequently in asthmatic children, with the highest impact in children with diagnosed asthma.

Table 3 Quality of life mean score of children and caregivers with undiagnosed asthma, diagnosed asthma and healthy controls

Quality of life score of children	Undiagnosed asthma		Diagnosed asthma		Healthy controls		*P* value
	n	Mean (95% C.I.)	*n*	Mean (95% C.I.)	*n*	Mean (95% C.I.)	
Emotions domain	103	6.6 (6.4–6.8)	67	6.4 (6.1–6.6)	153	7.0 (6.9–7)	<0.05[a, b, c]
Activity domain	90	5.6 (5.3–5.9)	54	5.1 (4.8–5.4)	93	6.9 (6.8–7)	<0.05[a, b, c]
Symptom domain	91	6.2 (6.0–6.4)	55	5.6 (5.3–5.9)	122	6.9 (6.9–7)	<0.001[a, b, c]
Combined domain	77	6.1 (5.8–6.3)	47	5.6 (5.4–5.9)	90	7.0 (6.9–7)	<0.05[a, b, c]
Quality of life score of caregivers							
Emotions domain	103	6.7 (6.6–6.8)	69	6.2 (5.9–6.4)	165	7.0 (6.9–7)	<0.001[a, b, c]
Activity domain	111	6.7 (6.6–6.8)	72	6.4 (6.2–6.6)	168	7.0 (6.9–7)	<0.05[a, b, c]
Combined domain	102	6.7 (6.6–6.8)	68	6.3 (6.1–6.5)	165	7.0 (6.9–7)	<0.001[a, b, c]

[a] Significant difference between undiagnosed asthma and diagnosed asthma
[b] Significant difference between undiagnosed asthma and healthy controls
[c] Significant difference between diagnosed asthma and healthy controls

Table 4 Annual absence from school due to respiratory symptoms

	Undiagnosed asthma, *n* (%)	Diagnosed asthma, *n* (%)	Healthy controls, *n* (%)	
Never	56 (50)	28 (40)	179 (93)	[a]
<1 week	37 (33)	20 (29)	13 (7)	[a]
1–2 weeks	12 (11)	21 (30)	0	[a]
3–4 weeks	5 (4)	1 (1)	0	[a]
>4 weeks	2 (2)	0	0	[a]

[a] *P* value <0.001

The major strength of our study is that, to our knowledge, this is the first population-based study which evaluated quality of life with standardized disease-specific questionnaires in children with undiagnosed asthma and diagnosed asthma and their caregivers and compared these children with healthy controls.

We found a higher frequency of BHR and a lower prevalence of wheeze in children with undiagnosed asthma than children with diagnosed asthma. There are several explanations for this finding. First, bronchial hyperresponsiveness was used in the definition of undiagnosed asthma, whereas bronchial hyperresponsiveness was not required in the definition of diagnosed asthma. Another explanation might be the dependence on recall of asthma symptoms. Recall by parents can be faulty. Furthermore, parents may not witness every asthma symptom a child experiences, which might explain that night-time symptoms are equal in children with undiagnosed asthma and diagnosed asthma. Nonetheless, patient report of asthma symptoms has long been a key factor in physician's decision making, and the survey mimics the questions they pose as part of assessment. Responses to the questionnaire are equally reliable as similar questions in the physician's office.

Our results on quality of life with the lowest score in diagnosed asthma suggest that children with undiagnosed asthma have a milder degree of asthma than children with diagnosed asthma. This is in agreement with quality of life scores reported by others. For example, our children with diagnosed asthma had quality of life scores similar to those in children with moderate asthma, and our scores for undiagnosed asthma were comparable with those in children with mild asthma as reported by Raat et al. [19] The relevance of mild asthma should not be underestimated. Fawcett et al. [7] showed that life-threatening exacerbations regularly occur in mild asthma. Moreover, mild asthma accounts for the majority of pediatric admissions.

The clinical interpretation of differences in quality of life is difficult because experience in their use is still limited. Juniper et al. [13] proposed a difference of 0.5 or higher as being clinically relevant for the PAQLQ. Knorr et al. [15] studied the effect of treatment in 6- to 14-year-old asthmatic children and observed a significant improvement of both FEV_1 and quality of life scores (with 0.4 for the emotional domain and 0.5 for the activity domain). In the light of these studies, our results suggest a clinically relevant impairment of quality of life in asthmatic children, irrespective of whether diagnosed or not. Until now, no reports are available on the clinical relevance of the parental scores of quality of life.

Our observations of lowest quality of life and highest symptom impact in diagnosed asthma compared with undiagnosed asthma seem in contradiction with observations on markers of airway obstruction (FEV_1, reversibility, BHR), which was highest in undiagnosed asthma.

Juniper et al. [14] reported a similar discrepancy. It is probable that clinical measures of airway status (such as airway calibre and markers of inflammation) evaluate a different component of asthma health status than quality of life. For instance, lung function is a static indicator in a variable disease, whereas quality of life scores reflect the patient's perceptions of the condition over a longer period of time. In addition, the stigma of being labelled as having asthma can be an explanation for the lower quality of life scores in children with diagnosed asthma. Further studies are needed to evaluate the effect of being diagnosed and medical treatment on quality of life in a community sample of undiagnosed asthma.

The following points may have affected our study results. First, we did not collect information on the reasons for non-response or the extent to which this may have biased our results. Second, bias may have been introduced if parents interpreted symptom questions different than the questionnaire definition [4, 16, 25]. Additionally, recall bias cannot be excluded since questions referred to a period of the past 12 months. For symptoms, we attempted to minimize bias by using the validated ISAAC questionnaire. One might argue that asthma-specific quality of life questionnaires are inappropriate to be used in healthy controls or in subjects without a diagnosis of asthma. However, the PAQLQ and PACQLQ also include questions on the impact of respiratory symptoms without making reference to 'asthma'. Therefore, we have considered them appropriate to use in children with undiagnosed asthma and healthy controls. Our observations of the highest scores in healthy controls that approximated the maximum value may be considered a confirmation. Furthermore, the disease-specific quality of life was significantly impaired in subjects who could be expected to experience impairments: the children with undiagnosed asthma. In addition, the results of more school absence in children with undiagnosed asthma compared with healthy controls supports the results of lower quality of life scores in children with undiagnosed asthma. A last comment addresses the selection of our patient groups. In this study, children with "asymptomatic airway reversibility" or "asthma symptoms

only" were excluded, because we aimed at a highest discrimination between asthma and healthy controls. Therefore, we included objective parameters (airway reversibility and BHR) for the definition of undiagnosed asthma. Nevertheless misclassification may have occurred since airway reversibility is variable present in asthma.

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